Regeneration

Guest Editors

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Preface

Models to crack the code of organ regeneration

In recent years, there has been a growing, widespread interest in tissue regeneration, with all its medical and social implications, such as, for example, the recovery from illness and wellbeing of humans. Yet, some of the most noticeable features of regeneration were discovered using a purely biological perspective with experimental biology on animal models. We are proud to introduce this Special Issue of *The International Journal of Developmental Biology (Int. J. Dev. Biol.)* on Regeneration Biology, which is devoted to the different animal models currently used to study regeneration. We also have tailored this Special Issue to include the different achievements that are today the state-of-the art in tissue and organ regeneration. The animal model perspective allows us to identify common and specific traits, summarize the most relevant advances, establish knowledge for the new "kids-on-the-block" and provide a framework to explore the open questions that researchers in the field are pursuing.

The question on how an organ can be replenished and reconstructed after injury has always fascinated mankind, as already reported by Greek mythology on liver regeneration. Many examples of regeneration were firstly characterized during the 18th century at the anatomical level in crayfish limbs by René Antoine Ferchault de Réamur, hydra by Abraham Trembley, annelids by Charles Bonnet, amphibians by Lazzaro Spallanzani and flatworms by Peter Simon Pallas. In the following 19th and 20th centuries, and until today, amphibians, hydra, teleosts, arthropods, flatworms and other model organisms, have been at the core of the search for the principles that govern regeneration. The driving force for these studies may well have come from pure scientific curiosity to understand the nature of regeneration. But, over the last few decades, scientists have started focusing on the potential of using regenerative therapies for medical purposes. With the incursion of stem cell biology and bioengineering in this scenario, a fundamental question has arisen: are all those "classical" animal models pertinent for regeneration studies in the 21st century? We are certainly convinced that animal model organisms are pivotal for the study of organ regeneration. There is still a lot to learn from nature on how to regenerate an organ. The combinatory knowledge of animal regeneration, stem cell biology and organoid technology can be fruitful in developing mechanisms for regenerative approaches in humans. Unveiling the cellular strategies and genetic programs that animals activate for repair and regeneration will provide us with a catalog of mechanisms that human tissues may activate to trigger a regenerative response. Indeed, progenitors, stem cells, transdifferentiation, or cell-cycle reentry are universally implicated in regeneration, as are key signaling pathways such as the Wnt or the role of reactive oxygen species (ROS). Furthermore, from a biological perspective, the robustness of the regeneration mechanisms can be demonstrated by responses that often are conserved through evolution.

There is a tendency to limit the exchange of information between scientists using the same animal model. This tendency to neglect information concerning other organisms has to be avoided and we need to favor the exchange of information between researchers using different animal models. Understanding regeneration as a dormant genomic program that has been conserved and can be reactivated upon the damage or stress is an attractive idea that merits further attention.

With the era of genome sequencing and emerging genome editing tools, many non-classical model organisms have now become amenable to genetic modification and allow studying the molecular basis of regenerative capacity throughout the animal kingdom. Furthermore, with increasing number of "omic" approaches to organ regeneration, we have also entered the big data era. It is now our chance to use this information to unravel conserved *versus* species-specific responses. In this sense, a good networking of scientists studying regeneration using different animal models, focusing on different organs and even more importantly, using different experimental approaches, is pivotal. Moreover, the synergy

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between the animal models and bioengineering designs is a promising approach for translational regenerative research.

Platforms such as the EMBO or the Gordon Conferences are aimed to precisely promote these interactions. Our wish is that this Special Issue can also contribute to this exchange of ideas between scientists interested in regeneration. The Issue starts with four introductory papers that summarizes its author's view on some animal models for regeneration research. One of them is a contribution on eye regeneration dedicated to Panagiotis Tsonis. Next, we introduce two interviews with Elly M. Tanaka and Ken Poss, both of whom are leaders of current regeneration research. All these introductory contributions are followed by a collection of review articles presenting the state-of-the-art of organ regeneration in several animal model systems ranging from sponges to mammals. You will discover "trending topics" in regeneration research and get to know better the "influencers" in the field. We are deeply indebted to all of the authors for their efforts and contributions and would also like to express our gratefulness to Said Messari for the cover art and to Josep Abril for his help with the organization of this Special Issue. We hope you enjoy finding out more about regeneration of the limb, heart, kidney, liver and much more!

Nadia Mercader and Florenci Serras
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